PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference VJR/B45310	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/06095	International filing date *(day/month/year)* 06.06.2003	Priority date *(day/month/year)* 11.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K39/00		
Applicant GLAXOSMITHKLINE BIOLOGICALS S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.12.2003	14.09.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Wagner, R Telephone No. +49 89 2399-7357

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/06095

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-43 as originally filed

Sequence listings part of the description, Pages

1-12 as originally filed

Claims, Numbers

1-27 as originally filed

Drawings, Sheets

1/13-13/13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 23-27

   because:

   ☒ the said international application, or the said claims Nos. 23-27 (regarding industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-7,9-27
	No:	Claims	1,8
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27
Industrial applicability (IA)	Yes:	Claims	1-22
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 23-27 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement.

2. Reference is made to the following documents:

   D1: WO 00/04149
   D2: WO 98/46769
   D3: WO 01/81577
   D4: Xu et al., Cancer Research 61, 1563-1568, 2001
   D5: Fong et al., The Journal of Immunology, Vol. 159, 3113-3117, 1997
   D6: Hodge et al., Int. J. Cancer, 63, 231-237.

3. Claim 1 is directed to an immunogenic composition comprising a xenogenic P501S polypeptide or an immunogenic fragment thereof. The subject-matter of claim 1 and of claim 8 as it stands is anticipated (Article 33(2) PCT) by D1 because discloses (page 63, example 8) that an immunogenic fragment of human P501S (also called L1-12) is injected into mice - i.e. the peptide is xenogenic to mice.

   In view of the definition given on page 5, lines 15-18 the claim should be limited for clarity reasons (Article 6 PCT) to xenogenicity regarding humans. If said definition was present in the claim the subject-matter of claim 1 would be novel (Article 33(2) PCT). The immunogenic composition comprising a xenogenic (for human) prostate-specific antigen is intended for the treatment of human prostate cancer. D2 discloses a treatment of human prostate cancer by a vaccine comprising a xenogenic (for human) prostate antigen. The difference between the

disclosure of D2 and claim 1 is the type of prostate antigen. The technical problem to be solved is the provision of an alternative prostate antigen for the immunogenic composition. As D3 indicates that P501S (also called PROST 3) can be used as a tumour vaccine against prostate cancer and as D4 proposes the use of P501S (called prostein) as a cancer vaccine (page 1568, last paragraph). and as the replacement of the antigen used in D2 by P501S does not generate any surprising effect, the subject-matter of claim 1 (being limited to P501S xenogenic in view of humans) would not involve an inventive step (Article 33(3) PCT).

In addition the subject-matter of claim 1 is strongly suggested by D3. D3 (page 34, second paragraph) discloses that P501S can be used in a vaccine in prostate cancer therapy. In this context D3 refers to two publications and states that the methods of said publications can be readily practised by employing P501S, or a fragment thereof. One of said two publication is D5, which discloses that a xenogenic prostatic acid phosphatase is able to produce an immunisation against a self-antigen. By applying the method of D5 using P501S as suggested by D3 the skilled person will inevitably arrive at the subject-matter of claim 1. In the second publication (D6) referred to by D3, non-human primates are vaccinated by a recombinant virus expressing human prostate-specific antigen. Thus, applying the method as carried out in D6 to the antigen P501S will also lead the skilled person to using a xenogenic form of P501S.

The same reasoning applies to the method of inducing an immune response against a human P501S in a human by using a xenogenic form of said human P501S protein. Therefore the method of claim 23 does not involve an inventive step (Article 33(3) PCT). The additional features of claims 24-27 do not confer an inventive step on the method (see also reasoning is sections 3-4 below for claims 25, 26 and 27.

In view of the preceding arguments and because the use of adjuvants and pharmaceutically acceptable carriers is common practice the process of claim 8, if it had been limited to xenogenicity regarding humans, would not involve an inventive step (Article 33(3) PCT).

4. In claim 2 the species from which the peptide is derived is limited to rat (Seq. Id. No. 1), cynomolgous monkey (Seq. id. No. 3) or mouse (Seq. Id. No. 10). Because both D3 and D4 disclose the sequence of human P501S, the cloning of

homologous polynucleotides and deriving of proteins in different species using primers derived from the human sequence does not require an inventive effort (Article 33(3) PCT). Therefore the additional features of dependent claims 2 and 3 do not confer an inventive step on the composition (Article 33(3) PCT).

5. As the use of adjuvants or the loading of an antigen in APCs are common practice the additional features of dependent claims 4-7 do not confer an inventive step on the immunogenic composition (Article 33(3) PCT).

6. The reasoning of section 3, leading to the lack of inventive step of an immunogenic composition comprising the rat homologous P501S protein applies to the rat homologous P501S protein itself (Seq. Id. No1) or fragments thereof (see also section 7 under further remarks) or polynucleotides (Seq. Id. No.2), vectors, host cells encoding the rat P501S protein. Therefore the subject-matter of claims 9-20 and the process for producing a rat P501S protein using a host cell expressing the corresponding nucleotide (claim 21) as well as the use of the rat polypeptide for producing an immunogenic composition (claim 22) for the treatment of prostate cancer does not involve an inventive step (Article 33(3) PCT).

FURTHER REMARKS

7. Claim 22 is not sufficiently disclosed (Article 5 PCT) and not supported by the description (Article 6 PCT) over the entire width of the claimed scope because the application does not give any indication which other non-prostate related diseases could be treated by a vaccine directed against a prostate-associated antigen.

8. Claim 13 as it stands is not clear (Article 6 PCT) because the expression immunogenic activity is too vague. In the light of the definition given in the description (page 6, lines 20-25) the intended immunogenic activity is the generation of cross-reactive antibodies, which react with the autologous human form of P501S. Said definition should have been incorporated in the claim.

9. The validity of the priority claimed for the present application could not be verified. In case the priority would not be valid the sequence published in October 2002 in the database EMBL under the accession number Q8K0H7 could be relevant for

the novelty and inventive step of claims 9-13.

10. For the assessment of the present claims 23-27 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.